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Original article

Comparative study between obstetric antiphospholipid syndrome and obstetric morbidity related with antiphospholipid antibodies

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ABSTRACT

Background and objectives: To compare clinical, laboratory, treatment and live birth rate data between women with aPL-related obstetric complications (OMAPS) not fulfilling the Sydney criteria and women fulfilling them (OAPS).
Materials and methods: Retrospective and prospective multicentre study. Data comparison between groups from The European Registry on Antiphospholipid Syndrome included within the framework of the European Forum on Antiphospholipid Antibody projects.
Results: 338 women were analysed: 247 fulfilled the Sydney criteria (OAPS group) and 91 did not (OMAPS group). In the OMAPS group, 24/91 (26.37%) fulfilled laboratory Sydney criteria (subgroup A) and 67/91 (74.63%) had a low titre and/or non-persistent aPL-positivity (subgroup B). Overall, aPL laboratory categories in OAPS vs. OMAPS showed significant differences: 34% vs. 11% ($p < 0.0001$) for category I, 66% vs. 89% ($p < 0.0001$) for category II. No differences were observed when current obstetric complications were compared ($p = 0.481$). 86.20% of OAPS women were treated vs. 75.82% of OMAPS ($p = 0.0224$), particularly regarding the LDA + LMWH schedule ($p = 0.006$). No differences between groups were observed in live births, gestational, puerperal arterial and/or venous thrombosis.
Conclusions: Significant differences were found among aPL categories between groups. Treatment rates were higher in OAPS. Both OAPS and OMAPS groups had similarly good foetal-maternal outcomes when treated. The proposal to modify OAPS classification criteria, mostly laboratory requirements, is reinforced by these results.

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Estudio comparativo entre síndrome antifisfolipídico obstétrico y morbilidad obstétrica relacionada con anticuerpos antifosfolípido

R E S U M E N

Fundamento Y objetivos: Comparar características clínicas, analíticas, tratamiento y tasa de hijos vivos entre gestantes con Síndrome Antifosfolípido Obstétrico (SAFO) y gestantes con morbilidad obstétrica relacionada con el síndrome que no cumplen los criterios de clasificación actuales.
Material Y métodos: Estudio observacional retrospectivo y prospectivo multicéntrico: datos de once hospitales terciarios europeos recogidos en el European Registry on Antiphospholipid Syndrome.
Resultados: Se analizaron 338 mujeres: 247 cumplían criterios de Sydney para SAFO (grupo OAPS), y 91 no (grupo OMAPS). En el grupo OMAPS, 24/91(26.37%) cumplían criterios analíticos, pero no clínicos para SAFO (subgrupo A) y 67/91(74.63%) presentaban títulos medio-bajos o títulos positivos no persistentes de anticuerpos antifosfolípido, con o sin cumplir criterios clínicos (subgrupo B). Se observaron diferencias significativas entre los 2 grupos en cuanto a las categorías analíticas: 34% vs. 11% ($p<0.0001$) para la categoría I y 66% vs. 89% ($p<0.0001$) para la categoría II, OAPS vs OMAPS, respectivamente. No se observaron diferencias significativas en cuanto a las complicaciones obstétricas ($p = 0.481$). El 86.20% del grupo OAPS recibió tratamiento vs.el 75.82% del grupo OMAPS ($p = 0.0224$). No se observaron diferencias en la tasa de hijos vivos, ni en la tasa de trombosis arterial y/o venosa gestacional y/o puerperal.
Conclusiones: Ambos grupos fueron muy homogéneos, excepto en cuanto a la distribución de las categorías analíticas y en la tasa de tratamiento. Ambos grupos mostraron buenos resultados al ser tratados. Los resultados respaldan la opinión de muchos expertos de tener que revisar los criterios de clasificación actuales del Síndrome Antifosfolípido Obstétrico.

Background and objectives

The antiphospholipid syndrome (APS) is an autoimmune systemic disorder characterised by an increased risk of vascular thrombosis and/or pregnancy morbidity, both associated with persistently – positive antiphospholipid/anticofactor antibody (aPL) tests according to the currently accepted Sydney criteria.[1] Thus, for APS diagnosis, at least one clinical criterion and one laboratory criterion are needed. APS is believed to be related to activation of the clot cascade with further thrombosis. Cases with poor obstetric outcomes, mainly recurrent first trimester miscarriage, foetal losses, stillbirth, early and severe preeclampsia leading to a preterm birth, but without a history of thrombosis, are known to have obstetric antiphospholipid syndrome (OAPS).[2] Although no complete agreement exists, there is evidence that laboratory markers, immunopathological pathways, treatment response, maternal complications and long-term follow-up may differ from those observed in APS outside the context of pregnancy.[3,4]

Consensus on the classification criteria for APS/OAPS permitted clinicians to standardise patient groups, but also generated controversy. In the last decade, a wide array of "non-criteria" obstetric morbidities and diverse non-classical aPL, low titres of accepted aPL, or other isotypes such as IgA, have been increasingly proposed.[5,6] Women with pregnancy complications highly suggestive of OAPS but with persistently low titres for aPL, and those with accepted laboratory aPL criteria but not presenting full obstetric morbidity criteria – e.g. two recurrent miscarriages or placental vascular insufficiency over 34 weeks of gestation – are classified as incomplete OAPS.[7,8] In addition, there is increasing discussion as to whether clinical cases with persistently negative titres for classical or non-classical aPL should be known as seronegative APS.[9,10] Several published manuscripts stressed the contrariness of both incomplete and seronegative APS.[7,11] Obviously, this raised practical clinical concerns regarding the classification and management of these women. Few studies have reported that women with persistent low-titre aPL positivity have obstetric outcomes comparable to the general population; thus, they may have good obstetric outcomes with or without treatment.[12,13] By contrast, a recent study showed that anticardiolipin antibody (aCL) and anti-β2glycoprotein-I antibody (anti-β2GPI) low-positivity titres accurately identify women with aPL-related pregnancy complications.[8,14–16] Given these considerations, some authors have claimed that the current diagnostic criteria are too restrictive and of limited use for clinical purposes, and have suggested redefining OAPS[8,15,17–19]; Thus, some women could be underdiagnosed – false-negative diagnosis – with further foetal maternal complications.

In 2014, the 14th International Congress on Antiphospholipid Antibodies Task Force Report on Obstetric APS concluded there is a paucity of data on several OAPS-related concerns and that new information should be obtained, mainly through randomised clinical trials and large series of patients recruited from multicentre registries. Moreover, they exposed the growing controversy on the clinical meaning of low titres of aPLs in pregnancy morbidity.[20]

Thus, and within the EUROAPS project framework, we decided to refer to this incomplete OAPS group as Obstetric Morbidity related to the Antiphospholipid Antibodies – OMAPS group. Herein, we present the results of the OMAPS group in terms of obstetric morbidity, foetal and maternal outcomes, laboratory results, treatment rates and live birth rates, compared with those of OAPS to shed some light on this matter, and provide further reasons for continuing to study this still debatable APS subset.

Materials and methods

Patients

Owing to the wide clinical spectrum of APS and strong evidence of the existence of different aPL-mediated pathogenic mechanisms between classical and obstetric forms of the syndrome, it was considered useful to create a single, homogeneous database in a multicentre European Registry where physicians could send, consult or insert patient data to facilitate and further understanding of several existing gaps associated with aPL-related obstetric syndromes, both in women fulfilling the Sydney criteria and those who did not.

From June 2010, the ad-hoc website and database have been accessible and ongoing. Since then, patient data have been included systematically, both retrospectively and prospectively, as stated previously [www.euroaps.org] and are now accessible

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